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PROGRESSIVE PARALYSIS OF THE EXTERNAL OCULAR MUSCLES, OR OPHTHALMOPLEGIA EXTERNA.

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DURING the fall of 1883, a patient was referred by Prof. D. B. St. John Roosa from his clinic at the Manhattan Eye and Ear Hospital to my service in the Department for Nervous Diseases of the same institution.

The patient, a male, aged 18 years, by occupation a bookkeeper, and of American birth and parentage, presented a group of symptoms which I had never met with before, and which was also unique in Dr. Roosa's extensive experience. They consisted of paresis of all the external muscles of both eyes, namely, the levator, the recti, and the oblique muscles; with complete preservation of function in the internal muscles (iris and ciliary muscles), along with a normal fundus and normal vision, except defects due to an error of refraction, and without evidence of lesions in any other nerve tract.

His history is as follows: About two years ago, his friends first noticed a sleepy expression of his eyes before he was himself aware of the drooping of the lids. The right eye became affected first; it was not until about six months ago that the left became decidedly affected. For two months before admission, increase in this bilateral ptosis was rapid, but never quite complete. He also observed a gradually progressive impairment of power in rotation

of the eyeball in all directions, until his eyes had become almost completely fixed, so that he was obliged to depend entirely upon rotation of the head to widen his field of view. He had not observed any failure of vision, and had been able to finish his collegiate studies, and afterward to write at bookkeeping many hours a day without difficulty. He never observed diplopia. He says he is perfectly well, with the exception of his eye trouble, and appears to regard that as of little consequence. He had, during his student life, an occasional headache, but never since. He acknowledges masturbation in former years, but denies positively the possibility of his ever having had syphilis or any venereal disease. There is no history of former sickness, except that during childhood he was said to have "kidney disease," and at ninth year fell down-stairs, striking his head. Syphilitic or nervous disease cannot be elicited from his family history.

Examination on admission: Double ptosis, most marked on right side, both eyes two-thirds closed; both eyes act equally in rotation, but the range is limited in all directions; pupils react to light and to accommodative movements; accommodation normal; fundus normal. Dr. J. B. Emerson, who made repeated examinations of his vision, found an irregular astigmatism in the right eye, and myopia in the left. Facial muscles act normally, and react normally to the faradic and galvanic currents; tongue and palatal muscles normal; deglutition and speech normal; nothing abnormal in sensory or motor distribution of the fifth, or of any other cranial nerves, except the third, fourth, and sixth pairs. Motility and sensibility of the trunk and extremities found entirely normal after the most thorough tests. No cardiac or pulmonary lesion. Patient has a healthy appearance except that he is somewhat pallid; has cold, wet palms, and a somewhat embarrassed manner. His mental condition appears sound. None of the visceral signs of locomotor ataxia, and no history of fulgurating pains.

The patient was treated for several weeks with galvanism (cathode on eye, anode on neck) without apparent effect, then for several weeks without electricity, but with tonic doses of nux vomica, also without apparent change in symptoms. He disappeared from the clinic for some weeks, and on his return was put upon increasing doses of potassium iodide (gr. xv., t. i. d., increasing gr. ij. per diem). About two weeks after beginning this treatment, the record states that patient appears to have slight increase in ptosis, but moves eyeballs somewhat better than before. Two weeks later, improvement in the movement of the eyes was more evident, particularly in the left eye; ptosis in the left eye being also less marked. Ninety grains of KI per dose had been reached at the time. No new symptoms had developed; vision, accommodation, reactions of iris, and the other functions of the body remaining, as at first, normal.

In attempting to explain the pathology of this, to me,

novel case, I reasoned as follows: We have impairment of function of the sixth, fourth, and part of the third nerves, on both sides. What is the nature and the seat of the lesion which will account for the involvement of these nerves, and, at the same time, allow the structure in the immediate vicinity to remain unimpaired? An intra-orbital lesion which involved the third nerve, would not permit the escape of the supply to the iris and ciliary muscle, nor would a lesion in any part of the trunk of this nerve, in its intracranial portion, account for it. We are, therefore, forced to conclude that the nuclei of origin are the parts involved. This view is strengthened from the fact that the affection is bilateral. Physiological and anatomical facts, notably the experiments of Gudden, and of Hensen and Voelcker, render plausible, if not demonstrable, the theory that the innervation of the sphincter iridis and of the ciliary muscle proceed from nuclei which, although in close proximity, are distinct from those giving origin to the remaining third nerve fibres which supply external ocular muscles. Our case would seem to be one in which the latter motor nuclei were involved, but not those for the internal ocular muscles. Assuming this, we are forced to another conclusion, namely, that the lesion cannot be a gross lesion. It is hardly possible to conceive of a tumor, a meningitis, an arteritis, or a focus of softening, affecting, bilaterally, nuclei so widely separated as the third, fourth, and sixth pair, and not at the same time involve the centres for the iris and ciliary muscle, the fifth or the seventh nerves, or other neural tracts, without we assume that several independent lesions exist, and have accidentally fallen upon the nuclei of a set of associated nerves. That such a marvel of chance should occur can hardly be entertained. It will be observed that all the muscles affected are associated to move the eye-ball and remove the lid, constituting within themselves a physiological system distinct from the functions of the iris and ciliary muscles which are more intimately connected with true vision. The most rational hypothesis, then, is that we have a progressive degeneration of this system.

primarily functional, but finally resulting in structural changes of a degenerative type similar to the processes in progressive muscular atrophy and in labio-glosso-pharyngeal paralysis. It is almost to be expected that this form of lesion should occasionally be found in these upper motor nuclei, as well as in the cord and medulla. While this view appears to be the most rational one, there are two others worthy of thought. Some parts of the nervous system resist the action of a pathological process in their vicinity, while neighboring parts have their functions interfered with thereby. It is barely possible that the oculo-motor centres might be affected by an inflammatory or neoplasmic process along the ventricular surface near these nuclei which other nerve centres might possibly resist entirely or for a long period of time, and such a theory may account for cases in which affections of the motor nuclei are simply initiatory to a more widespread involvement of neighboring centres in rapid succession. Another still more plausible view is, that vascular changes have resulted in numerous minute hemorrhagic extravasations, those falling within motor nuclei inducing therein degenerative changes and more disastrous results than where they fall in conducting tracts or in sensory areas which are supposed to have a greater number of pathways open to impressions that usually traverse them. Such minute hemorrhages are frequently found after acute febrile diseases, also in nerve centres distant from some focus of disease in other regions of brain or cord. In my own cases, however, there is little to substantiate either of these views, while the slowly progressive course, symmetrical and systematic distribution of the paralysis, together with the absence of other signs of disease, point more conclusively to the view I have advanced.

I was obliged to confess to those to whom I broached this view that I was not aware of any autopsies that would comfirm it, nor, in fact, of any published account of such cases. Not long after my examination of this case, however, I found in Ross' valuable text-book an ac-

count of a similar group of symptoms under the heading, Progressive Paralysis of the Ocular Muscles, which up to that time had escaped my notice, as well as the papers of von Graefe and Hutchinson on which his description was based, and on reading Hutchinson's paper, I found a similar view of the pathology of such cases expressed as that stated above in my own case.

Mr. Jonathan Hutchinson's paper was published in the "Medico-Chirurgical Transactions" for 1879. In one of his autopsies, made by Dr. Gowers, a lesion was found in the ocular motor nuclei resembling that found in progressive muscular atrophy.

Before referring again to Hutchinson's cases, the history of a second case will be presented which, by one of those strange coincidences in which rare events run in groups, came to my notice a few months after the first, for which I am indebted to Dr. F. M. Wilson, of Bridgeport, Conn., Assistant Surgeon to the Manhattan Eye and Ear Hospital, who recognized its identity with the former case, and kindly brought the gentleman, a private patient, for me to examine. His notes of observations upon the the case are as follows:

J. E. D., aged 29, farmer, began in January, 1883, to see double. At first, the diplopia was intermittent, "would come on once or twice a day, but would last only a few minutes." About the last of April, this double vision became constant. Has now, June 2d, paresis of right internal rectus, R.V. = $\frac{20}{20}$, L.V. = $\frac{20}{20}$. Reads No. 1 (J.) with either eye up to six inches. About the middle of September, the lids began to droop, and in November the double vision ceased. Jan., 1884, there was marked ptosis, and the eyes were fixed so that they could not be moved in any direction. R.V. = $\frac{20}{20}$, L.V. = $\frac{20}{20}$. No. 1 (J.) read at six inches. No other symptoms. He denies all venereal trouble, and states that he "has not been sick a day since he was fourteen years old." Potassium iodide was ordered, gr. x. t. i. d., increasing gr. i. per day. Faradism to the eyes. June 9th, 1884; he has had the faradic current almost every day since January. The potassium iodide was gradually increased up to gr. lxxx. t. i. d., which he is now taking. There has been a slow, gradual improvement. He can now move his eyes horizontally through an arc of about forty-five degrees, and up and down through an arc of about thirty degrees. There has been some improvement in the ptosis, but not much; at no time since November, 1883, has he had diplopia. Up to the

1st of May, his eyes moved slowly and with effort. They now move quickly to the limit, and no amount of effort carries them any farther.

As a result of my examination, no defect was found in any other nerve distribution than the sixth, fourth, and external muscular supply of the third nerves on both sides, except a suspicion that the upper or orbital group of the facial muscles responded to electrical excitation not quite as actively as upon the opposite side; the difference was so slight, however, that not much stress could be placed upon it. Both cases here reported were exhibited by Dr. Roosa at meetings of the New York Ophthalmological Society, and, I am informed, failed to elicit any new cases, except one which Dr. Kipp, of Newark, said he had observed. On writing to Dr. Kipp, asking if his case corresponded to those here reported, in exhibiting paralysis of the external muscles of both eyes only, he was unable to give me exact notes, but thought his case was the same in character.

To Mr. Hutchinson we are indebted for that convenient classification of paralytic affections of the eye, or ophthalmoplegia, into those affecting the extrinsic or external muscles of the eye (*ophthalmoplegia externa*), and those affecting the intrinsic or internal muscles of the eye, namely, the iris and ciliary muscle (*ophthalmoplegia interna*), the latter group being divided *into cycloplegia*, or paralysis of the ciliary muscles, and *iridoplegia*, or paralysis of the radiating and circular fibres of the iris, again subdivided into *myosis paralytica* and *mydriasis paralytica*.

Under the title "Ophthalmoplegia Externa, or Symmetrical Immobility (Partial) of the Eyes, with Ptosis," Mr. Hutchinson reports seventeen cases, to which he refers, as follows: "They are characterized by a very peculiar group of symptoms. Drooping of the eyelids, so as to give to the face a half-asleep expression, is usually first, and it is soon accompanied by weakness of all the muscles attached to the eyeball, so that the movements of the latter become much restricted, or even wholly lost. The con-

dition is usually bilateral, though it is not always in exactly in the same degree on the two sides. Its symmetry probably denotes that it is of cerebral origin. It by no means always happens that all the ocular muscles are alike affected, or that they are attacked symmetrically, still it is a very marked feature of the malady that the muscles fall in groups, and not singly. Non-symmetrical paralysis of single ocular muscles is, of course, very common, especially in connection with syphilis and locomotor ataxia, but such cases are to be distinguished from those which I am now describing; first, by the fact of non-symmetry; secondly, by the early completeness of the paralysis; and thirdly, by the ease with which very frequently they are cured. In the majority of them there is, perhaps, good reason to suspect that a gumma in the nerve track is the cause. In the symmetrical cases now under consideration, however, the changes probably begin centrally; they are usually slow in progress, and are often difficult of relief. They agree with the single nerve cases, in that they occur chiefly in those who have had syphilis. Although I have ventured to speak of immobility of the eyeballs, I by no means wish to imply that it is usually complete; on the contrary, incompleteness in the degree of paralysis is almost as marked a feature as is the tendency to affect many muscles at the same time. Although the eyelids droop, there is seldom complete ptosis; great limitation of the range of motion of the eyelids is more common than fixation. The degree, however, varies with the stage, and at a later period, the paralysis may be absolute. The third, fourth, and sixth nerves are, of course, those which are involved, but not infrequently in the early stage one or more of these may wholly escape. Occasionally, the optic nerve itself is involved, and sight is lost. I am making these statements from a limited number of cases, for the condition is but seldom seen."

Concerning their probable pathology, he says: "The cases in question are probably closely allied in nature to what is known as progressive muscular atrophy, their peculiar features being that only one special set of muscles

(or rather nerves) is at first attacked. We have probably in them a very close parallel to the so-called bulbar paralysis, the labio-glosso-pharyngeal paralysis of Duchenne. In it, as in ophthalmoplegia externa, central degenerative changes occur, and the result is the paralysis of a set of associated muscles. It may be plausibly conjectured that the initial lesion is inflammatory of the nuclei of the affected nerves, which, in a slowly serpiginous manner, creeps from place to place along certain definite anatomical paths. Within certain limits, its directness of spreading and its progressive tendency may vary in different cases, but, speaking generally, the cases are remarkably the same in their features. In exceptional instances, definite symptoms of locomotor ataxia are present, and in others still more rare, the fifth nerves or the seventh, or even the eighth may be involved."

Curiously enough, although Mr. Hutchinson calls these, cases of ophthalmoplegia externa; of his seventeen cases, in only three is it positively stated that both the iris and ciliary muscles were not involved; in a fourth, they were normal on one side and involved on the other. He admits, however, that the ophthalmoplegia interna is "often, indeed, usually associated with symmetrical ophthalmoplegia externa." While the involvement of the internal muscles does not exclude the possibility of the lesion being that which the Hutchinsonian pathological theory involves, still we cannot be as certain that a neuritis, consequent upon basal meningitis, ependemitis, or neoplasms, may not have been the cause, particularly as in several of his cases other cranial nerves and nerve-tracts were involved; in some cases, the optic, producing atrophy; in others involvement of the fifth, and also involvement of the motor or sensory functions of the extremities and trunk. It is in the closely-defined character of the symptoms, therefore, involving an associated set of functions only, that the two cases whose histories I have reported are of such interest and value as supporting Hutchinson's view. We cannot tell what new involvements these cases might have developed if left to themselves, or may yet exhibit not-

withstanding treatment. The extension to other motor nuclei in the central gray matter, either above or below these first involved, would not be inconsistent with the theory of systematic degeneration, in fact goes to confirm Hutchinson's view that these cases form a part of the clinical history of progressive muscular atrophy.

Paresis of any of the external ocular muscles, pointed out by Duchenne as one of the earliest signs of tabes dorsalis, naturally comes to mind in the consideration of such cases. Of Hutchinson's cases, seven out of the seventeen presented some symptoms suggestive of this disease. Unfortunately, the pupillary phenomena, discovered by Argyle Robertson, of reflex immobility to light, with preserved mobility to accommodative reflexes, had not been described when Hutchinson's paper was written. Its frequency and importance as an early sign of tabes dorsalis is now well recognized. In a number of Hutchinson's cases, the sphincter pupillæ were paretic; in others, fixed and of medium size, but whether to light alone is not stated; the involvement of the optic nerve and the ciliary muscles and the external muscles introduces complications which render it difficult to estimate the value of the findings. In the cases which I have reported, however, we have no pupillary impairment and no optic atrophy, the pupillary reflexes are preserved, there is no history of the characteristic pains of tabes dorsalis, and no history of of syphilis. Yet it is possible that time may show a development of these signs.

It would consume too much time to analyze all of Hutchinson's cases, the greater number of which, as already shown, are more complicated than those reported in this paper. The case with an autopsy, however, demands notice, as it is the one on which he founds the pathology of the disease, grouping it with bulbar paralysis of the progressive muscular atrophy type, while to my own mind it presents more of the clinical feature of a case of tabes dorsalis. It is but fair to state that the author himself says that this particular case "in part resembles locomotor ataxia, and in part progressive muscular atrophy."

Male, æt. 48, gardener; in 1869 had slight paresis of right sixth nerve (slight convergence and diplopia); right pupil rather larger than the other; near vision defective from weak accommodation; distant vision nearly perfect. Four years later, in right eye barely perception of light, left eye scarcely reads No. 20; could not abduct either eye; right eye habitually crossed inwards. No positive paralysis of other ocular muscles, but all acted feebly; sleepy look from drooping of lids, but can lift lids with effort Left interni weaker than rest. Optic disk very pale, arteries and veins much reduced in size. He had been liable to attacks of severe pain in his forehead, sometimes for a week at a time or more. Cramp in the legs for seven or eight years at night; bowels somewhat constipated. At this time the pupils did not react in the least; left, of medium size; right, larger; no habitual headache. Mercury pushed to ptyalism without definite benefit. In 1874, pupils motionless, external recti paralyzed, all others imperfect. Bowels very costive, sensation of tightness around abdomen like a strap; numbness of skin over abdomen and on face, slight on hands, a little on the feet. Later, aggravation of symptoms. He became absolutely blind; had a sort of "choking fit." Still later, his extremities failed him, were usually "icy cold," and he became bed-ridden, suffered dreadful pains in his head, and was frequently out of his mind; could eat, speak, and swallow well. He died in this condition seven years after the commencement of the symptoms. No history of syphilis, but eldest child, æt. 20, had notched teeth, and had had a most characteristic condition of syphilitic keratitis.

Autopsy, in which the brain only was obtained. Examined by Dr. Gowers.

Brain somewhat softened from commencing decomposition, cranial nerves examined in fresh state, pons and medulla after hardening. Nothing abnormal in convolutions or in corpora striata; hyperæmic patches in left lenticular nucleus; posterior tubercle of thalamus a little softer and smaller than normal; olfactory nerves normal; optic nerve and chiasma uniformly gray, fair consistence, optic tracts also gray; whitish striations in pons. Microscopical examination of nerves and tracts showed fat globules and degenerating fibres, but also a large number of healthy fibres. Third nerves smaller than natural, gray and translucent, very few healthy fibres, some fibres undergoing degeneration; numerous connective-tissue nuclei. In crura cerebri the tracts of fibres of origin are indicated by numerous connective-tissue fibres; scarcely any nerve fibres could be seen. In their nuclei beneath nates, disappearance of almost all of the multipolar nerve cells, two or three only to be seen in each section. A few cells of some size, but without processes, were seen, also very abundant minute angular cells not larger than connective-tissue nuclei.

Fourth nerve: No trace to be seen; their nuclei beneath testes presented a similar degeneration to that found in the third nerve nuclei.

Fifth nerve: Upper fibres of root appeared healthy, but lower fibres had a gray appearance, granular degeneration and segmentation; within pons little recognizable alteration in fibres of nerve; nuclei for most part normal; nuclei of motor roots of fifth normal.

Sixth nerve: Reduced to fine gray threads, with scarcely a nerve fibre to be seen, also in tracts of origin within pons. The so-called conjoined nuclei presented general degeneration, most of the large cells had disappeared, and only granules, nuclei, and small angular cells remained.

Facial nerves: Perfectly normal in the trunks and roots of origin within pons; nerves and nuclei of the auditory, glosso-pharyngeal, pneumogastric, and hypoglossus normal; peri-vascular erosions found throughout medulla, pons, and corpora quadrigemina large and numerous. In the lower part of floor of the fourth ventricle some areas of disintegration in gray substance just beneath the lining membrane, and the surface, partly from this cause, is more or less irregular. One such area appeared to have been caused by a small hemorrhage. No indication was found of pressure upon nerves, or of any acute changes in their nuclei. Dr. Gowers also remarks that the disintegration and connective-tissue changes are those continually met with in the gray matter of the cord in progressive muscular atrophy in the nerves and their nuclei of origin.

As the cord was not obtained, we cannot determine the question whether sclerosis of the posterior columns of the cord was not also present. Buzzard has called attention to these cases of symmetrical involvement of the ocular muscles as a part of the clinical history of tabes dorsalis. Thus these two great systemic degenerative diseases of the nervous system, the one affecting principally the motor nuclei of the central gray column, the other involving simply the sensory tracts, would seem to merge into each other in many cases.

I have not attempted to review the great mass of neurological and ophthalmological literature pertaining to this subject with any degree of thoroughness. Similar cases are no doubt hidden under names which give the searcher no clue to their existence. It may be mentioned, however, that von Graefe, in 1869, reported a case of symmetrical paralysis of the external ocular muscles only. The attack was sudden, of comparatively brief duration, and terminated in recovery. It is of interest, in that he attributed it to a basal meningitis.

H. Breusgin has reported the following remarkably interesting ease:

A female, æt. 25, without previous illness, developed in September, 1875, diplopia from paresis of the right sixth nerves. In the spring of 1876, bilateral ptosis and slow but regularly progressive paresis of all the external ocular muscles of the left eye occurred, with perfect preservation of vision, power of accommodation and pupillary reaction, and a normal fundus. The lids could not be completely closed, indicating involvement of the orbicularis palpebrarum. In 1878, the right eye became affected; in 1879, both bulbi were immovable. The speech began to be decidedly affected, while the lips and tongue were freely active, and the palate exhibited nothing abnormal to sight. Yet the patient had a decidedly nasal speech, and the consonants p and b could not be pronounced distinctly. Difficulty in deglutition also followed, and distinct emaciation followed, which finally became very great; speech becoming unintelligible, and deglutition performed only with the greatest difficulty, death at last resulting from syncope. Up to the last moment, the iris and ciliary muscles remained normal. There was no autopsy.

The author groups his case with those of progressive bulbar paralysis, and the lesion, he believes, was some destructive process, be it a neoplasm or a focus of softening in the floor of the fourth ventricle and acqueduct of Sylvius, destroying the nuclei of the affected nerves: namely, the third, fourth, sixth nerves, and knee of the facial whose first branch was affected. He explains the escape of the third nerve supply to the internal ocular muscles on the supposition that nuclei for these muscles are situated more anterior (cephalad) than the other nuclei, which view he bases on Hensen and Voelcker's experiments to that effect. He also refers to Alfred Graefe's view that some anomalous anatomical variation may be present in those cases in which the iris and ciliary muscle escape. The author cites three similar cases reported by Foerster, whose paper was inaccessible to me (Med. Soc., Breslau, 1878).

Note.—The publication of the preceding paper has been purposely delayed since its presentation to the American Neurological Association, in order to watch the progress of the cases reported. I am able to say that now, after an interval of two years and a half, the condition of both

cases remains practically unchanged, but slight improvement has occurred, and what is of the utmost interest, there are no new symptoms or indications of the extension of the disease to other nerve tracts; in this respect these cases seem to be unique. The manuscript has been left as written in June, 1884, which accounts for the absence of reference to recent literature.